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10/522,137

01/19/2005

Kenichi Yamashita

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SUITE 800

WASHINGTON, DC 20006-1021

EXAMINER

POHNERT, STEVEN C

ART UNIT

PAPER NUMBER

1634

MAIL DATE

DELIVERY MODE

10/15/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                                      |   |  |
|------------------------------|--------------------------------------|---|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/522,137 | <b>Applicant(s)</b><br>YAMASHITA ET AL. |  |
|                              | <b>Examiner</b><br>Steven C. Pohnert | <b>Art Unit</b><br>1634                 |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 7/22/2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1 and 4 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 4 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 January 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### **Continued Examination Under 37 CFR 1.114**

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/22/2008 has been entered.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, THIS ACTION IS MADE FINAL even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

Art Unit: 1634

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

### **Claim Status**

This action is in response to papers filed 7/22/2008.

The papers filed have amended claims 1 and 4. The amendment has corrected typographical errors, but has not altered the scope of the claims.

The instant response has presented the same arguments presented in the after final amendment that was filed on 4/22/2008 and entered on 6/18/2008.

As noted in the advisory action of 6/18/2008 the double patenting rejection has been withdrawn as 10/527987 has been abandoned.

Claim 2 was canceled in the after final amendment that was entered on 6/18/2008.

This action is Final.

### **Claim Rejections - 35 USC § 102-maintained**

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Wolinsky, et al (WO 1994/00598, published January 6, 1994).

With regards to claims 1 and 4, Wolinsky et al teaches a method of analyzing a specimen by detection of DNA sequences by flow cytometry (see abstract). Wolinsky et al teaches a solution containing FITC-tagged oligonucleotide probes was added to samples in which PCR amplification had been done (see page 12, 1st paragraph). Wolinsky teaches the samples were allowed to hybridize (form a complex) and then analyzed by flow cytometry (see page 12, 2nd paragraph). Flow cytometry is analysis of a sample in laminar flow through a microflow channel. Wolinsky et al further teaches detection of the complex by excitation of the fluorescent dyes (FITC and propidium iodine (PI)) (see page 13 1st paragraph). Wolinsky thus teaches a method of analyzing a DNA sample (specimen) by causing a solution containing the DNA and a solution containing fluorescent probe to promote diffusion by laminar flow and detect the presence of the specimen molecule by altered diffusion relative to the specimen molecule and probe molecules.

Wolinsky teaches the instrument was calibrated using calibration beads before each assay and a standard curve was produced (see page 13). Wolinsky et al thus analysis of the degree of diffusion was carried out in reference to a calibration curve.

### **Response to arguments**

The following arguments are essentially the same as provided in the advisory action of 6/18/2008. The arguments have been modified slightly in hopes of improving clarity and support has been added to demonstrate that flow cytometry is laminar flow.

The response traverses the instant rejection and asserts that the method of Wolinsky is different is different than the instant claims.

The response asserts that the solution hybridization and flow cytometric analysis are not identical to the instant invention, as Wolinsky teaches the cells and probes are combined prior to analysis. The response on page 4 continues by asserting that step 1 of claims 1 and 4 require, "at least two solutions" are passed through the microchannel. These arguments have been thoroughly reviewed but are not considered persuasive as the claim requires a solution containing (comprising) (1) specimen molecules and a (2) solution containing fluorescent probes. Thus a single solution that comprises a specimen and a solution with a fluorescent probes comprises the solution that is being passed through the microflow channel as the claims do not preclude pre-mixing. Step (1) of the claims do not require the two solutions be mixed in the microchannel or even that a complex be formed, but merely a complex is capable of being formed and that at some point in the micro flow channel there is laminar flow. An amendment to the claims to require the mixing of two solutions in a micro flow channel may overcome the art of Wolinsky if it is supported by the instant specification. Thus as Wolinsky teaches the broadest reasonable interpretation of step (1) of instant claims, Wolinsky does anticipate this step.

The response further asserts, "In step (1) of the present invention, it is indispensable to form a laminar flow in the micro flow channel. On the other hand, a particulate dispersion, a particle in which is used as a solid-phase carrier, is allowed to pass through a fine flow channel in the cytometric analysis of Wolinsky et al., but there is no utilization of any fluid dynamic characteristics capable of forming a laminar flow as required in the present invention. In case of the method of Wolinsky et al., a turbulent

Art Unit: 1634

flow of the dispersion is more effective than a laminar flow". These are arguments of counsel that have not been supported by evidence.

First, MPEP 716.01(c) makes clear that "The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant."

This should not be construed as an invitation for providing evidence. As further stated in the MPEP 716.01 regarding the timely submission of evidence:

A) Timeliness.

Evidence traversing rejections must be timely or seasonably filed to be entered and entitled to consideration. In re Rothermel, 276 F.2d 393, 125 USPQ 328 (CCPA 1960). Affidavits and declarations submitted under 37 CFR 1.132 and other evidence traversing rejections are considered timely if submitted:

(1) prior to a final rejection,

(2) before appeal in an application not having a final rejection, or

(3) after final rejection and submitted

(i) with a first reply after final rejection for the purpose of overcoming a new ground of rejection or requirement made in the final rejection, or

- (ii) with a satisfactory showing under 37 CFR 1.116(b) or 37 CFR 1.195, or
- (iii) under 37 CFR 1.129(a).

Further it is noted that while Wolinsky does not specifically recite laminar flow, the teachings of Wolinsky do repeatedly teach the use of flow cytometry. As the response has asserted that Wolinsky's method uses turbulent flow, the examiner presents the teachings of Edwards et al (Current Opinion in Chemical biology (2004) volume 8, pages 392-398) that flow cytometry is laminar flow.

Flow cytometry enables discrete measurements of optical signals (e.g. fluorescence and light scatter) from single particles such as cells or beads. Sample particles are hydrodynamically focused into a laminar flow so that single particles pass through a laser beam sequentially. The subsequent optical signal characteristics are recorded in real time.(Page 392, 2<sup>nd</sup> column, 1<sup>st</sup> full paragraph).

The teachings of Edwards are merely being used to refute the unsupported assertions of the response and are not to be construed as part of the instant rejection.

The response continues, "in the step (2) of the present invention, the complex is selectively brought into diffusion. In contrast, no change is formed in diffusion coefficient in the cytometric analysis of Wolinsky et al. wherein particles as a solid carrier are dispersed into a solution to prepare a dispersed solution." In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., Wolinsky's method does not result in a change in diffusion coefficient are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the



Art Unit: 1634

specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Thus the method of Wolinsky does detect the diffusion of the hybridized probe complex with specimen relative to the non-hybridized probes.

The response further asserts, "in the step (3) of the present invention, analysis is carried out by detecting the degree of diffusion of the complex and comparing the result to a predetermined calibration curve. In the cytometric analysis of Wolinsky et al., however, no change is formed in the diffusion coefficient so that analysis utilizing the degree of diffusion cannot be carried out in Wolinsky et al." As stated above and the advisory action of 6/18/2008, there is no claim limitation requiring a change in a diffusion coefficient.

Further the response appears to assert the examiner has not given weight to the discussion of selective diffusion in paragraph 34 of the specification. These arguments have been thoroughly reviewed but are not considered persuasive as the cited section of the specification teach, "diffusion can be selectively accelerated." Thus the specification is teaching how diffusion can selectively be accelerated not defining a term. Further the use of the "can" suggests this is an embodiment and not limiting.

The response further asserts that Wolinsky's calibration curve is different than the calibration curve of the instant specification as the instant invention allows for quantitative detection. The specification does not set forth a limiting definition of quantitative analysis and Wolinsky's method allows for the detection of the presence or absence of the probe molecule complex. Wolinsky thus teaches quantitative detection.

The response concludes the arguments to the 102 of Wolinsky by asserting, " the calibration curve of the instant invention cannot be employed for calibration of instruments." In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the calibration curve of the instant invention cannot be used for calibration of instruments) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Further this assertion again appears to be arguments of counsel that has not been supported by any evidence on the record.

**Claim Rejections - 35 USC § 103- Maintained**

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

Art Unit: 1634

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1 and 4 rejected under 35 U.S.C. 103(a) as being unpatentable over Wolinsky, et al (WO 1994/00598, published January 6, 1994) in view of Chee et al (US Patent 6355431, published March 12, 2002).

This rejection is being presented to the interpretation that the claims require the determination of the amount of specimen molecules by comparison to the calibration curve.

With regards to claims 1 and 4, Wolinsky et al teaches a method of analyzing a specimen by detection of DNA sequences by flow cytometry (see abstract). Wolinsky et al teaches a solution containing FITC-tagged oligonucleotide probes was added to samples in which PCR amplification had been done (see page 12, 1st paragraph). Wolinsky teaches the samples were allowed to hybridize (form a complex) and then analyzed by flow cytometry (see page 12, 2nd paragraph). Flow cytometry is analysis of a sample in laminar flow through a microflow channel. Wolinsky et al further teaches detection of the complex by excitation of the fluorescent dyes (FITC and propidium iodine (PI)) (see page 13 1st paragraph). Wolinsky teaches the instrument was calibrated using calibration beads before each assay and a standard curve was produced (see page 13). Wolinsky thus teaches a method of analyzing a DNA sample (specimen) by causing a solution containing the DNA and a solution containing fluorescent probe to promote diffusion by laminar flow and detect the presence of the

Art Unit: 1634

specimen molecule by altered diffusion relative to the specimen molecule and probe molecules.

Wolinsky does not explicitly teach comparing the results of the assay to a calibration curve obtained by the use of immunobright calibration beads to quantitatively analyze the sample.

However, Chee et al teaches quantitation of nucleic acids based on the signals generated by the sample of interest that is then compared to a calibration curve to measure the concentration of the analyte (column 58, lines 25-40).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of Wolinsky by combining it with the quantitation methods of Chee with a reasonable expectation of success as both Wolinsky and Chee are drawn to detecting nucleic acids. The skilled artisan would have been motivated to combine the teachings of Wolinsky and Chee because Chee teaches the comparison analyte data to calibration curves allows the artisan to determine the amount of analyte present. The combination Chee and Wolinsky would result in a method to quantitate the amount of a target analyte in a sample by use of a calibration curve.

### **Response to arguments**

The following arguments are essentially the same as provided in the advisory action of 6/18/2008. The arguments have been modified slightly in hopes of improving clarity.

Art Unit: 1634

The response further asserts that the combination of Wolinsky and Chee do not render the instant claims obvious. The response re-asserts that Wolinsky does not teach selective diffusion, this argument has been address previously in this office action.

The response asserts that one of skill in the art could not combine the teachings of Wolinsky and Chee because Chee is directed to comparing analyte data to calibration curves to determine the amount of analyte that is present. The response asserts this is different than determining the degree of diffusion of the instant invention. This argument has been thoroughly reviewed but is not considered persuasive as the rejection relies on Wolinsky teachings the determination of diffusion of a specimen probe complex and probe molecules and the response agrees that Chee teaches a calibration curve and determining the amount. Thus the combination of Chee and Wolinsky renders the narrow interpretation of the claims as obvious.

The response further asserts that Chee's method requires the use of solid phase carriers that are dispersed into a solution and that probes and carriers are fixed in Chee's methods. These arguments have been thoroughly reviewed but are not considered persuasive as Chee is being referenced for teaching of calibration curves and thus arguments to Chee's solid carriers are moot. The response in the first full paragraph of page 6 admits that Chee teaches the use of calibration curves to determine amounts and has provided no evidence that the teachings of Wolinsky and Chee would not work.

First, MPEP 716.01(c) makes clear that "The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant."

This should not be construed as an invitation for providing evidence. As further stated in the MPEP 716.01 regarding the timely submission of evidence:

A) Timeliness.

Evidence traversing rejections must be timely or seasonably filed to be entered and entitled to consideration. In re Rothermel, 276 F.2d 393, 125 USPQ 328 (CCPA 1960). Affidavits and declarations submitted under 37 CFR 1.132 and other evidence traversing rejections are considered timely if submitted:

- (1) prior to a final rejection,
- (2) before appeal in an application not having a final rejection, or
- (3) after final rejection and submitted
  - (i) with a first reply after final rejection for the purpose of overcoming a new ground of rejection or requirement made in the final rejection, or
  - (ii) with a satisfactory showing under 37 CFR 1.116(b) or 37 CFR 1.195, or

(iii) under 37 CFR 1.129(a).

The response further asserts that the claimed method has overcome the difficulties associated with hybridization prior to analysis as taught by Chee. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., hybridization prior to analysis as taught by Chee) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The claims require the formation of a complex, which in the art of nucleic acid is hybridization. Further the claims do not exclude hybridization prior to analysis, but a solution comprising two components the specimen molecules and a solution containing a fluorescent probe molecules. Thus Wolinsky teaches a solution containing specimen molecules and probes.

The response concludes the arguments to the combination of Wolinsky and Chee, "because both these references require hybridization." The response appears to be asserting the claimed method does not require hybridization. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the instant method does not require hybridization) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Thus for the reasons of record the rejection is maintained.

### **Summary**

No claims are allowed.

### **Conclusion**

5. This is a RCE of applicant's earlier Application No. 10522137. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven C. Pohnert whose telephone number is (571)272-3803. The examiner can normally be reached on Monday-Friday 6:30-4:00, every second Friday off.



Art Unit: 1634

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Steven Pohnert

/Sarae Bausch/  
Examiner, Art Unit 1634